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## Adult Stem Cell Therapy and Heart Failure, 2000 to 2016: A Systematic Review.

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### Public Summary:

Stem cell therapy is a promising treatment strategy for patients with heart failure, which accounts for more than 10% of deaths in the United States annually. Despite more than a decade of research, further investigation is still needed to determine whether stem cell regenerative therapy is an effective treatment strategy and can be routinely implemented in clinical practice. **OBJECTIVE:** To describe the progress in cardiac stem cell regenerative therapy using adult stem cells and to highlight the merits and limitations of clinical trials performed to date. **EVIDENCE REVIEW:** Information for this review was obtained through a search of PubMed and the Cochrane database for English-language studies published between January 1, 2000, and July 26, 2016. Twenty-nine randomized clinical trials and 7 systematic reviews and meta-analyses were included in this review. **FINDINGS:** Although adult stem cells were once believed to have the ability to create new heart tissue, preclinical studies suggest that these cells release cardioprotective paracrine factors that activate endogenous pathways, leading to myocardial repair. Subsequent randomized clinical trials, most of which used autologous bone marrow mononuclear cells, have found only a modest benefit in patients receiving stem cell therapy. The lack of a significant benefit may result from variations in trial methods, discrepancies in reporting, and an overreliance on surrogate end points. **CONCLUSIONS AND RELEVANCE:** Although stem cell therapy for cardiovascular disease is not yet ready for routine clinical application, significant progress continues to be made. Physicians should be aware of the current status of this treatment so that they can better inform their patients who may be in search of alternative therapies.

### Scientific Abstract:

**Importance:** Stem cell therapy is a promising treatment strategy for patients with heart failure, which accounts for more than 10% of deaths in the United States annually. Despite more than a decade of research, further investigation is still needed to determine whether stem cell regenerative therapy is an effective treatment strategy and can be routinely implemented in clinical practice. **Objective:** To describe the progress in cardiac stem cell regenerative therapy using adult stem cells and to highlight the merits and limitations of clinical trials performed to date. **Evidence Review:** Information for this review was obtained through a search of PubMed and the Cochrane database for English-language studies published between January 1, 2000, and July 26, 2016. Twenty-nine randomized clinical trials and 7 systematic reviews and meta-analyses were included in this review. **Findings:** Although adult stem cells were once believed to have the ability to create new heart tissue, preclinical studies suggest that these cells release cardioprotective paracrine factors that activate endogenous pathways, leading to myocardial repair. Subsequent randomized clinical trials, most of which used autologous bone marrow mononuclear cells, have found only a modest benefit in patients receiving stem cell therapy. The lack of a significant benefit may result from variations in trial methods, discrepancies in reporting, and an overreliance on surrogate end points. **Conclusions and Relevance:** Although stem cell therapy for cardiovascular disease is not yet ready for routine clinical application, significant progress continues to be made. Physicians should be aware of the current status of this treatment so that they can better inform their patients who may be in search of alternative therapies.